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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/995,691	11/29/2001	Joon Shik Shin	0662-0163P	9800

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EXAMINER	
KRISHNAN, GANAPATHY	

ART UNIT	PAPER NUMBER
1623	6

DATE MAILED: 10/25/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/995,691	SHIN ET AL.	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-4 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-4 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Objections

Claim 3 is objected to because of the following informalities: Claim 3 recites, "novel material developed by the inventors" in parentheses. This should be removed. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 1 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of arthritis and ruptured disc does not

reasonably provide enablement for prevention of arthritis, osteoporosis and ruptured disc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

These factors include:

(A) The breadth of the claims;
(B) The state of the prior art
(C) The level of predictability in the art;
(D) The amount of direction provided by the inventor;
(E) The existence of working examples; and
(F) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims

Claim 1 is drawn to a compound of formula (I) as an agent for the treatment and prevention of arthritis, osteoporosis and ruptured disc. The scope of the claims is seen to include the administration of the said composition to a healthy subject, and the subsequent exposure to the conditions that would cause the said diseases, wherein the said compound prevents said exposure from manifesting itself in the subject exposed. The claim fails to provide methodological steps.

The state of the prior art

The prior art cited by the applicants disclose treatment for arthritis and osteoporosis. However, there is no disclosure of potential arthritic, osteoporotic or disc rupture preventive activity of the instantly claimed compound seen in the prior art. The prior art appears to be silent with regard to preventive procedures recognized by the skilled artisans in the field.

The level of predictability in the art

The examiner acknowledges the probability and predictability that the administration of the said compound would have a reasonable expectation of success for treating arthritis, osteoporosis or rupture of disc. There is not seen sufficient data to substantiate the assertion that the said conditions may be prevented by the use of the compound instantly claimed. Currently, the art does not provide compounds and/or therapeutic regiments to prevent (cure and eradicate) arthritis, osteoporosis or ruptured disc.

The amount of direction provided by the inventor

The instant specification is not seen to provide enough guidance that would allow a skilled artisan to extrapolate from the disclosure and the examples provided to enable the use of the said compound to prevent arthritis, osteoporosis and rupture of disc. The specification also fails to direct the skilled artisan in correlative prior art procedures which might provide the basis for an advance in treating the said conditions which induces prevention.

The existence of working examples

The working examples set forth in the instant specification is drawn to data involving rats, cells and a patient. The skilled artisan in this field would not extrapolate the preventive efficacy of the compound claimed or the use of the same in the preventive methods from the examples provided. The disclosure does not show the prevention of the said conditions. The

disclosure does not provide guidance or reference art recognized examples to support the prevention of any conditions.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure

Indeed, in view of the information set forth, the instant disclosure is not seen to be sufficient to enable prevention of the said conditions with the compound set forth in the claim. A skilled artisan would not extrapolate the preventive efficacy from the results disclosed in the instant specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 provides for the use of a compound of formula (I), but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 1-4 recite a compound represented by structural formula I. The formula has a dashed line on one of the carbons in the five membered ring. It is not clear if the dashed line represents a methyl group or whether a substituent is missing at the end of the dashed line. For the purpose of prosecution of this case it is assumed that the dashed line represents a methyl

group. Also it is not clear what the substitution "Glc" represents. If it represents glucose then the structure of glucose should be incorporated in the formula or it should be indicated in the claim what "Glc" represents.

Claim 4 as recited is not clear. It appears that a process for preparing a compound of formula I where R_2 is hydrogen which is obtained by the hydrolysis of the compound of formula I wherein R_2 is cinnamoyl. If this is what is claimed, then Claim 4 should be restated to recite:

A process for preparing a compound of formula (I) wherein R_2 is hydrogen atom, which has a more potent pharmacological activity, characterized in that the compound of formula (I) wherein R_2 is cinnamoyl is hydrolyzed to give the compound of formula (I) in which R_1 represents hydrogen atom or alkyl group and R_2 represents hydrogen atom. For the purpose of prosecution of this case it is assumed that a process for making compound of formula (I) wherein R_2 is hydrogen and which is obtained by hydrolysis of compound of formula (I) wherein R_2 is cinnamoyl group is what is claimed.

JOINT INVENTORS

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chrubasik et al (The Pain Clinic, vol. 11, no. 3, pp. 171-178) in combination with Recio et al (Planta Medica, vo. 60, no. 3, pp. 232-234), Stumpf et al (USPN 6280737), Wheatley et al (GB 2335919) and Kikuchi et al (Chem. Pharm. Bull. 1983, vol. 31, no. 7, pp. 2296-2301).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4 are drawn to a compound of formula (I) as an agent for prevention and treatment of arthritis, osteoporosis and ruptured disc, pharmaceutical composition containing an effective amount of the compound of formula (I) with a pharmaceutically acceptable auxiliary, diluent, isotonic agent, preservative, lubricant and solubilizing aid and other ingredients; and a

process for making compound of formula (I) wherein R_2 is hydrogen and which is obtained by hydrolysis of compound of formula (I) wherein R_2 is cinnamoyl group.

Chrubasik et al teach the use of harpagoside, the principal component of Harpagophytum procumbens (see figure 1, pg. 172) for treatment of osteoarthritis in patients (see pg. 174, clinical studies).

Recio et al teach the use of harpagoside to reduce inflammation which is a condition associated with arthritis (see fig. 1 on bottom left of page. 23; middle paragraph and table 2 on the right column of page 233).

However Chrubasik and Recio do not teach pharmaceutical compositions containing the compound of formula (I).

Stumpf et al teach the use of an extract containing 5% harpagoside for the treatment of rheumatoid arthritis (see col. 6, claims 3 and 8). Stumpf also discloses pharmaceutical compositions (col. 6, claim 7) containing harpagoside and discloses that the extracts may be usedin drug preparations by adding conventional adjuvants (see col. 2, lines 42-45). This disclosure shows the compounds in the same class as Chrubasik et al are known to be included in pharmaceutical compositions.

Wheatley et al teach the use of tablets containing harpagophytum extract and maltodextrin as an excipient for treating inflammatory conditions (see page 6, and claims 8-14). This shows that hapagophytum extract can be combined with multiple excipients to make pharmaceutical compositions.

However, Chrubasik, Recio, Stumpf and Wheatley do not teach a process for preparing the compound of formula (I) wherein R_2 is hydrogen and which is obtained by hydrolysis of compound of formula (I) wherein R_2 is cinnamoyl group.

Kikuchi et al teach the preparation of a compound of formula (I) wherein R_2 is hydrogen by the hydrolysis of a compound where R_2 is p-coumaroyl group (see pg. 2297, first paragraph, lines 6-7, hydrolysis of compound 3 to afford 1, Chart 1). The only difference is that in the compound of the instant claim 4 a cinnamoyl group is hydrolysed. In compound 3 of the reference a coumaroyl group (group has a hydroxy substitution in the benzene ring) is hydrolyzed. The process yields the same product whether a cinnamoyl or a coumaroyl group is hydrolyzed.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the prior art to use compound of formula (I) for the treatment of arthritis, for the preparation of a pharmaceutical composition and preparing compound of formula (I) wherein R_2 is hydrogen by hydrolysis of cinnamoyl group since the teachings of the prior art are seen to disclose the same.

One of ordinary skill in the art would be motivated to do so because the compound of formula (I) in particular, which has a hydroxy group in the 5 and 6 position of the ring are more potent in reducing edema (see Recio et al, discussion, pp. 234) and are hence useful in treating edema in addition to arthritis, osteoporosis and ruptured disc. Compound of formula (I) can also be used to make additional structural modifications in an attempt to enhance their potency.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 703-305-4837. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 703-308-4624. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

GK
October 21, 2002

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
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